

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	What is the Association of Renin-Angiotensin-Aldosterone System Inhibitors with Covid-19 Outcomes: Retrospective Study of Racially Diverse Patients?
<b>AUTHORS</b>	Khodneva, Yulia; Malla, Gargya; Clarkson, UAB; Fu, Richard; Safford, Monika; Goyal, Parag; Oparil, Suzanne; Cherrington, Andrea; Jackson, Elizabeth A.; Willig, James

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Yuan Hong Zhejiang University School of Medicine, Neurosurgery
<b>REVIEW RETURNED</b>	08-Aug-2021

<b>GENERAL COMMENTS</b>	<p>The authors have presented a retrospective analysis involving 1024 racially diverse patients with COVID-19. They found that the use of ACEI/ARB was associated with a reduced risk of in-hospital mortality after adjustment. The main novelty of the study comes from study of racially diverse patients. There are still some issues that should be addressed.</p> <ol style="list-style-type: none"><li>1. Some data in table 1 (Vital signs, Laboratory data) is inconsequential and is not well discussed in the passage. This part should be omitted.</li><li>2. Confounder is always a potential issue in an observational study. The authors try to balance the confounders. But the data after adjustment should be included in the table.</li><li>3. In Discussion, the authors claimed that “Our study expands on previous findings by demonstrating both safety and reduction in Covid-19-related mortality...”. As we know, there were many studies has reached the similar conclusion that ACEI/ARB was associated with a reduced risk of in-hospital mortality. The authors should include some of these studies.</li><li>4. “HIV” is a kind of virus, while AIDS is a kind of disease. This should be corrected all along the manuscript. In addition, the disease caused by HIV should be included in the abbreviations of the table.</li><li>5. Abstract: “in-hospital mortality” should be “In-hospital mortality”.</li></ol>
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<b>REVIEWER</b>	E Abinaya Chettinad Academy of Research and Education, Pharmacology
<b>REVIEW RETURNED</b>	24-Oct-2021

<b>GENERAL COMMENTS</b>	<ol style="list-style-type: none"><li>1. There are many typographical errors and spelling mistakes throughout the manuscript.</li><li>2. In the results section (both in abstract and in the article, it was mentioned that 356 (35.6%) participants were taking RAAS</li></ol>
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	inhibitors whereas in table 1 in page number 18, it is shown that 365 participants were taking ACEi/ ARB. Hence, it needs modification. 3. The article may be accepted after these corrections.
<b>REVIEWER</b>	Raja Chandra Chakinala Guthrie Robert Packer Hospital, Hospitalist Medicine
<b>REVIEW RETURNED</b>	07-Nov-2021
<b>GENERAL COMMENTS</b>	<p>Suggestions: Needs proof reading for correcting minor spelling mistakes at some places. Page 4: Strength and limitations were not adequately explained. Page 5: Most of the description under outcomes and main exposure seems out of place. Please, limit the discussion to only “outcomes and main exposure” and mention the rest of it (for eg: trend in cases, delayed strategy) under study participants and procedures or a separate subheading.</p> <p>Overall, a well written paper discussing an important aspect of COVID-19 patient care. At the beginning of the pandemic, there has been concerns about using ACEi/ARBs in COVID-19 patients attributing to the increased ACE2 receptor expression leading to severe disease vs potential adverse effects, which however has later been proven to be not the case. This article not only addresses this concern but also points out the favorable outcomes with continuing ACEi/ARBs in COVID-19 patients.</p>

#### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

1. Some data in table 1 (Vital signs, Laboratory data) is inconsequential and is not well discussed in the passage. This part should be omitted.

*Response:* These data were removed from the table 1.

2. Confounder is always a potential issue in an observational study. The authors try to balance the confounders. But the data after adjustment should be included in the table.

*Response:* Thank you for your comment. The table 2 and 3 present point estimates from the multivariable adjusted models. We have updated the way results presented to clarify this.

3. In Discussion, the authors claimed that “Our study expands on previous findings by demonstrating both safety and reduction in Covid-19-related mortality...”. As we know, there were many studies has reached the similar conclusion that ACEi/ARB was associated with a reduced risk of in-hospital mortality. The authors should include some of these studies.

*Response:* Some data on the reduced mortality risk from COVID-19 among patients on ACEi/ARB have been included into the Discussion section now.

4. “HIV” is a kind of virus, while AIDS is a kind of disease. This should be corrected all along the manuscript. In addition, the disease caused by HIV should be included in the abbreviations of the table.

*Response:* “HIV” abbreviation has been rephrased as “HIV positive status” as none of these patients had AIDS. HIV has been added to the abbreviation list.

5. Abstract: “in-hospital mortality” should be “In-hospital mortality”.

*Response:* This has been corrected.

Reviewer: 2

Dr. E Abinaya, Chettinad Academy of Research and Education

Comments to the Author:

1. There are many typographical errors and spelling mistakes throughout the manuscript.

*Response:* This has been corrected.

2. In the results section (both in abstract and in the article, it was mentioned that 356 (35.6%) participants were taking RAAS inhibitors whereas in table 1 in page number 18, it is shown that 365 participants were taking ACEi/ ARB. Hence, it needs modification.

*Response:* Thank you for your comment. The data in the table are correct. We corrected the typo in the text.

3. The article may be accepted after these corrections.

Reviewer: 3

Dr. Raja Chandra Chakinala, Guthrie Robert Packer Hospital

Comments to the Author:

Suggestions:

Needs proof reading for correcting minor spelling mistakes at some places.

*Response:* This has been corrected.

Page 4: Strength and limitations were not adequately explained.

*Response:* This section has been revised.

Page 5: Most of the description under outcomes and main exposure seems out of place. Please, limit the discussion to only “outcomes and main exposure” and mention the rest of it (for eg: trend in cases, delayed strategy) under study participants and procedures or a separate subheading.

*Response:* This has been corrected.

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Yuan Hong Zhejiang University School of Medicine, Neurosurgery
<b>REVIEW RETURNED</b>	08-Jan-2022
<b>GENERAL COMMENTS</b>	i think this version is acceptable for publication